Attorney's Docket No. 045600/274147

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Carozzi *et al.*	Confirmation No.:	2147
Appl No.:	10/781,979	Group Art Unit:	1638
Filed:	February 19, 2004	Examiner:	Anne R. Kubelik
For:	AXMI-008, A DELTA-ENDOTOXIN GENE AND METHODS FOR ITS USE		

Mail Stop Amendment
Commissioner for Patents
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RESPONSE TO RESTRICTION REQUIREMENT

This is in response to the Office Action dated November 4, 2005, in which the Examiner has required restriction between Group I, namely Claims 1-11, 19, 22 and 24, drawn to a nucleic acid, vectors, host cells, plant cells, plants and seeds comprising it, and a method of using it to produce a protein; Group II, namely Claims 12-13, 15-18 and 20-21, drawn to a protein, compositions comprising it, and a method of using it to kill a pest; and Group III, namely Claim 14, drawn to an antibody. Upon election of a Group, Applicants are additionally required to select a single nucleotide sequence or amino acid sequence for said Group, as appropriate. Applicants hereby provisionally elect with traverse to prosecute the claims of Group I (Claims 1-11, 19, 22 and 24), as drawn to SEQ ID NO:1, and expressly reserve the right to file divisional applications or take such other appropriate measures deemed necessary to protect the inventions in the remaining claims.

Group I is drawn to isolated nucleic acid molecules encoding delta-endotoxin polypeptides. It is submitted that a search of the nucleotide sequence of this nucleic acid molecule will reveal information relevant to the polypeptide sequence. As the Examiner is aware, the DNA and amino acid sequences are related. If one knows the DNA sequence, one can readily determine the amino acid sequence of the polypeptide. Thus, Groups I (Claims 1-11, 19 22 and 24) and II (claims 12-13, 15-18, and 20-21) should be considered together. MPEP 803 sets forth that "If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." Applicants submit that the consideration of Groups I and II together will not be a burden on the Examiner. The issues surrounding the nucleic acid molecule

together will not be a burden on the Examiner The issues surrounding the nucleic acid molecule and the polypeptide claims are essentially the same and thus should be considered together. In fact, these groups are sometimes considered together by other examiners, indicating that it is not a serious burden on the Examiner to search and examine the two groups together.

Applicants further request that the Restriction Requirement be reconsidered and SEQ ID NOS:2, 4 and 6 be searched with the nucleic acid of SEQ ID NO:1 under 37 CFR § 1.142. 37 CFR § 1.142 requires that the inventions be "independent and distinct." According to MPEP 802.01, "independent" requires that there is no disclosed relationship between the two or more subjects disclosed. The relationship of SEQ ID NOS:1, 2, 4 and 6 does not meet this standard. The nucleotide sequences of SEQ ID NOS:2 and 4 are structurally and functionally related to SEQ ID NO:1 in that SEQ ID NOS:2 and 4 represent fragments of SEQ ID NO:1 and encode biologically active delta-endotoxin polypeptides (represented by SEQ ID NOS:3 and 5, respectively). The fragments of SEQ ID NOS:2 and 4 represent alternate start sites for the nucleotide sequence of SEQ ID NO:1. The nucleotide sequence of SEQ ID NO:6 is structurally and functionally related to SEQ ID NO:1 in that SEQ ID NO:6 encodes a delta-endotoxin auxiliary protein (represented by SEQ ID NO:7) that may have pesticidal activity, or may be important in facilitating expression of the delta-endotoxin protein encoded by SEQ ID NO:1. This structural and functional relationship is set forth in the specification as follows:

> Bacterial genes, such as the AXMI-008 gene of this invention, quite often possess multiple methionine initiation codons in proximity to the start of the open reading frame. Often, translation initiation at one or more of these start codons will lead to generation of a functional protein. These start codons can include ATG codons. However, bacteria such as *Bacillus sp.* also recognize the codon GTG as a start codon, and proteins that initiate translation at GTG codons contain a methionine at the first amino acid. Furthermore, it is not often determined *a priori* which of these codons are used naturally in the bacterium. Thus, it is understood that use of one of the alternate methionine codons may also lead to generation of delta-endotoxin proteins that encode pesticidal activity. For example, an alternate start site for a delta-endotoxin protein of the invention may be at nucleotide 177 of SEQ ID NO:1. Translation from this alternate start site results in the amino acid sequence found in SEQ ID NO:5. These delta-endotoxin proteins are encompassed in the present invention and may be used in the methods of the present invention.
>
> In addition, there may be one or more additional open reading frames in the disclosed nucleotide sequences that encode one or more delta-endotoxin-

> associated proteins. By "delta-endotoxin-associated protein" is intended a protein encoded by a nucleotide sequence disclosed herein using an alternate open reading frame than that used by the delta-endotoxins of the present invention. Proteins such as these are known in the art as helper proteins, stabilizing sequences, or delta-endotoxin-associated proteins. These delta-endotoxin-associated proteins may have pesticidal activity, or may be important in facilitating expression of delta-endotoxin proteins....These delta-endotoxin-associated proteins are encompassed by the present invention, and may be used in the methods disclosed herein, either alone or in combination with known delta-endotoxin proteins. In one embodiment, the delta-endotoxin-associated protein has the amino acid sequence found in SEQ ID NO:7 and is encoded by the nucleotide sequence of SEQ ID NO:6. (page 5, paragraph 3)

> Nucleic acid molecules that are fragments of these delta-endotoxin or delta-endotoxin-associated protein-encoding nucleotide sequences are also encompassed by the present invention. By "fragment" is intended a portion of the nucleotide sequence encoding a delta-endotoxin protein or delta-endotoxin-associated protein. A fragment of a nucleotide sequence may encode a biologically active portion of a delta-endotoxin or delta-endotoxin-associated protein, or it may be a fragment that can be used as a hybridization probe or PCR primer using methods disclosed below. Nucleic acid molecules that are fragments of a delta-endotoxin or a delta-endotoxin-associated nucleotide sequence comprise at least about 15, 20, 50, 75, 100, 200, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1100, 1200, 1300, 1400, 1500, 1600, 1700, 1800, 1900, 2000, 2100, 2200, 2300, 2400, 2500, 3000, 3500, 4000, 4500, 5000, 5500 nucleotides, or up to the number of nucleotides present in a full-length delta-endotoxin or delta-endotoxin-associated protein-encoding nucleotide sequence disclosed herein (for example, 5980 nucleotides for SEQ ID NO:1, 2082 for SEQ ID NO:2, 2073 for SEQ ID NO:4, or 1686 for SEQ ID NO:6), depending upon the intended use. (page 9, paragraph 3)

Furthermore, the nucleic acid molecules of SEQ ID NOS:1, 2, 4 and 6 are related one to another by a high degree of homology within a nucleotide range of the sequence. SEQ ID NO:2 is 100% homologous to nucleotides 168-2249 of SEQ ID NO:1, and SEQ ID NO:4 is 100% homologous to nucleotides 177-2249 of SEQ ID NO:1. SEQ ID NO:6 is 100% homologous to nucleotides 2311-3994 of SEQ ID NO:1. Applicants submit herewith a table showing the alignment of SEQ ID NOS:1, 2 and 4 (Appendix A) and the alignment of SEQ ID NOS:1 and 6 (Appendix B) with the consensus sequence displayed in reverse text (white letters on black

background). Applicants submit that a search of each of these sequences will reveal information relevant to all of the nucleic acid molecules identified in the claims.

Applicants submit that the consideration of all of the identified nucleic acid molecules will not be a burden on the Examiner as the issues surrounding the nucleic acid molecules are essentially the same and thus should be considered together. In fact, claims to more than one species of nucleotide sequence are frequently considered together by other examiners when the sequences share a high level of homology, indicating that it is not a serious burden to search and examine these sequences together.

For these reasons, it is requested that the Examiner reconsider and examine Groups I and II together, as well as examine each sequence within Groups I and II. Applicants request that the Examiner at least reconsider and examine SEQ ID NOS:1, 2, 4 and 6. Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned so that further examination of this application can be expedited.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those, which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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I hereby certify that this paper is being facsimile transmitted to the US Patent and Trademark Office at Fax No. (571) 273-8300 on the date shown below.

Lynda-Jo Pixley — Nov. 30, 2005
Lynda-Jo Pixley — Date